GSK Experiences in Life Cycle Inventory and Assessment

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Corporate Environment, Health, Safety and Sustainability
* Now Lockheed Martin

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Washington, DC. June 2009
Outline

- About GSK
- LCI/A in GSK:
  - CtG LCA of an API
  - LCI/A in the GSK Sustainability Tools
    - Solvent Selection Guide
    - FLASC
    - Green Technology Guide
    - WRAP
  - Other applications
- Future Work on LCI/A at GSK
Who are we?

- We are one of the world’s leading producers of prescription medicines, vaccines and consumer healthcare products

- 6.3% of global pharmaceutical sales

- Total company sales: £23.2 billion/ $43 billion

- We lead the way in respiratory and anti-viral medications and vaccines

- Over 100,000 GSK people in 117 countries

Each year GMS produces over 4 billion packs
What do we do?

- Every second...
  We distribute more than 35 doses of vaccine

- Every minute...
  More than 1,100 prescriptions are written for GSK products

- Every hour...
  We spend more than £300,000 ($562,000) to find new medicines

- Every day...
  More than 200 million people around the world use a GSK brand toothbrush or toothpaste

- Every year...
  Our factories produce 9 billion Tums tablets, 6 billion Panadol tablets and 600 million tubes of toothpaste
Our flagship products
GSK EHS Plan for Excellence

Sustainability in Environment, Health and Safety Plan for Excellence

- Engages through collaboration
- Embraces GSK principles
- Aligns with the GSK key business drivers
- Sets strategic objectives
- Sets EHS themes year by year to sharpen focus
- Builds our momentum
LCI/A Program in GSK

Sustainable by Design
Sustainability Tools:
- FLASC
- WRAP
- SSG
- GTG

- APIs
- Bioprocesses
- Technologies
- Solvents
- Packaging
- Waste Treatment
- Respiratory Devices
Cradle-to-gate LCA of a GSK API

- **Functional Unit**: 1 kg of API
- **GSK process studied** has **7 stages**
- **26 materials** directly used in GSK process
- To make these 26 materials requires the manufacture of a total of **119 materials** (125 including GSK’s intermediates)

**Cradle-to-Gate Analysis involved:**
- **Process**:
  - Materials
  - Energy
  - Transportation
- **Treatment**:
  - wastewater treatment,
  - incineration, and
  - Solid waste disposal.

**Source**: Jimenez-Gonzalez, Curzons, Constable, Cunningham, 2004. Int J LCA 9(2) 114-121
Methodology

Total Gate-to-Gate pre-treatment emissions = Process + Energy emissions

Materials required for a process, chemical trees with GSK-LCA metrics

Source:
LCA of API pre-treatment results

Cradle-to-gate pre-treatment contributions:
Solvents, Chemicals, Internal

- Eutrophication (PO4-3-eq.)
- Acidification (SO2-eq)
- GHG (CO2-eq)
- POCP (kg-et)
- TOC (kg)
- Energy (MJ)
- Total cradle materials (kg)

Bar chart showing contributions from Chemicals, Solvents, and Internal sources for various impact categories.
Key Learnings of LCI/A of an API

- **Solvent use (excluding incineration)** is the major contributor to:
  - Energy (ca. 75%)
  - Resource utilisation (about 80%)
  - Photochemical Ozone Creation Potential (ca. 70%)
  - Green House Gases (about 50%)
  - associated impacts when compared to GSK processes, transport and manufacture of other raw materials.

- The energy required to incinerate solvent wastes not recovered is approximately equivalent to a total of:
  - 60% of the energy used to produce the API
  - 50% of the post-treatment Green House Gas emissions

- **WW treatment** does not significantly increase overall life cycle profile.

- **Transport** contribution to overall impacts is low.
LCI/A in GSK’s Sustainability Tools
Welcome to the Eco-Design Toolkit!

Eco-Design Toolkit is a component of the myEHS Community and supports GSK's Plan for Excellence.

New Interactive Solvent Select Guide and Information

Click on a solvent name for portal to data on physical properties/THS, Life Cycle, Separability.

- The presence that there is more information if you know how to use it.

Additional Solvents

<table>
<thead>
<tr>
<th>SOLVENT</th>
<th>WPIR</th>
<th>Impact/Ethicality</th>
<th>Life Cycle</th>
<th>GHS use</th>
<th>GHS recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethylene glycol</td>
<td>4</td>
<td>9</td>
<td>3</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>1,6-Hexanediol</td>
<td>6</td>
<td>3</td>
<td>3</td>
<td>5</td>
<td>3</td>
</tr>
</tbody>
</table>

Fast Lifecycle Assessment for Synthetic Chemistry (FLASC)

A new component of the Eco-Design Toolkit.

FLASC® is located at greenroute.gsk.com

FLASC uses a “life cycle” approach to evaluate the environmental consequences of new or existing processes based around the input materials used. It quantifies the energy and materials used in their manufacture, as well as greenhouse emissions, and potential environmental impacts.

- Evaluate your options
- Identify process improvements
- Identify the best platforms for deployment

Your assessments will be tracked via your LSN ID: <insert ID>
Solvent Selection Guide

Life Cycle - cradle to gate environmental impacts for manufacture

Click on a solvent name for portal to data on physical properties/EHS, Life Cycle and Separability.

<table>
<thead>
<tr>
<th>SOLVENT</th>
<th>Waste</th>
<th>Impact</th>
<th>Health</th>
<th>Safety</th>
<th>Life cycle</th>
<th>GMS use</th>
<th>GMS recovery</th>
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<td>8</td>
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<td></td>
<td></td>
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<tr>
<td>1-Butanol</td>
<td>5</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td>5</td>
<td>Ir</td>
<td>Ir</td>
</tr>
<tr>
<td>Diethylene glycol butyl ether</td>
<td>5</td>
<td>7</td>
<td>10</td>
<td>9</td>
<td>7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-Ethyl hexanol</td>
<td>5</td>
<td>7</td>
<td>8</td>
<td>7</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isoamyl alcohol</td>
<td>7</td>
<td>6</td>
<td>8</td>
<td>6</td>
<td>7</td>
<td></td>
<td></td>
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<tr>
<td>Methanol</td>
<td>7</td>
<td>6</td>
<td>7</td>
<td>7</td>
<td>9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>t-Butyl acetate</td>
<td>7</td>
<td>10</td>
<td>7</td>
<td>7</td>
<td>7</td>
<td></td>
<td></td>
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<tr>
<td>Propyl acetate</td>
<td>6</td>
<td>7</td>
<td>8</td>
<td>7</td>
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<td>Isopropyl acetate</td>
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<td>8</td>
<td>8</td>
<td>7</td>
<td>6</td>
<td>A,U,S</td>
<td>A,S</td>
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<td>Methyl acetate</td>
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<td>Dimethyl carbonate</td>
<td>3</td>
<td>7</td>
<td>8</td>
<td>7</td>
<td>8</td>
<td></td>
<td></td>
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<tr>
<td>p-Xylene</td>
<td>8</td>
<td>2</td>
<td>7</td>
<td>5</td>
<td>7</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Source: Eco-Design Toolkit

Methodology:
- Curzons AD, Constable DJC, Cunningham VL. 1999 Clean Products and Processes 1:82-90 and
- Jiménez-González C, Curzons AD, Constable DJC, Cunningham VL. 2005 J. of Clean Tech. and Env..Pol 7:42-50,
For example, clicking in 2-propanol we get...
Streamlined LCI/A in GSK: FLASC™

Fast Lifecycle Assessment for Synthetic Chemistry (FLASC)

FLASC uses a "life cycle" approach to evaluate the environmental consequences of new or existing processes based around the input materials used. It quantifies the energy and materials used in their manufacture, as well as emissions released, and potential environmental impacts.

FLASC will:

- Compare or benchmark processes/routes and identify the greenest option
- Provide guidance and identify the materials that have the biggest impact

For information on how the site was developed, and should be used and all the benefits it will deliver, see the Background section.

Your assessments will be tracked via your LAN ID:

Enter FLASC  Administration Module

Source: Eco-Design Toolkit
Methodology: Curzons, Jimenez-Gonzalez, Duncan, Constable, Cunningham, 2007, IJLCA, 12(4)272-280
**Streamlined LCI/A in GSK: FLASC™**

**FLASC** = **Fast Life cycle Assessment for Synthetic Chemistry**

The % value shown is the improvement (reduction in environmental impacts) compared to the worst route selected.

**Used in GSK to:**
- Evaluate greenness
- Compare routes
- In R&D Green Metrics
- In Manufacturability Criteria
- Process-Related Materials Reviews
- In CEO Award entries
### Measure of Chemistry Efficiency

<table>
<thead>
<tr>
<th>Material</th>
<th>Weight/kg</th>
<th>Classification</th>
<th>Solvent Score</th>
<th>Reactant</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRL9950</td>
<td>1.4</td>
<td>Average Complex Organic</td>
<td>(N/A)</td>
<td></td>
</tr>
<tr>
<td>Dichloromethane</td>
<td>101.9</td>
<td>Solvent</td>
<td>703.1</td>
<td></td>
</tr>
<tr>
<td>Ethanol</td>
<td>5.9</td>
<td>Solvent</td>
<td>26.9</td>
<td></td>
</tr>
<tr>
<td>Ethyl acetate</td>
<td>7.4</td>
<td>Solvent</td>
<td>33.4</td>
<td></td>
</tr>
<tr>
<td>HCl</td>
<td>4.9</td>
<td>General Inorganic</td>
<td>(N/A)</td>
<td></td>
</tr>
<tr>
<td>Isopropanol</td>
<td>6.5</td>
<td>Solvent</td>
<td>33.8</td>
<td></td>
</tr>
<tr>
<td>Methane sulphonyl chloride</td>
<td>2.3</td>
<td>Average Simple Aliphatic</td>
<td>(N/A)</td>
<td></td>
</tr>
<tr>
<td>NaOH</td>
<td>2.0</td>
<td>Metal Cation Inorganic</td>
<td>(N/A)</td>
<td></td>
</tr>
<tr>
<td>Potassium carbonate</td>
<td>6.5</td>
<td>Average Metal Cation Inorganic</td>
<td>(N/A)</td>
<td></td>
</tr>
<tr>
<td>Sodium bicarbonate</td>
<td>1.0</td>
<td>Average Metal Cation Inorganic</td>
<td>(N/A)</td>
<td></td>
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<tr>
<td>Sodium ethyl xanathate</td>
<td>2.0</td>
<td>Average Complex Organic</td>
<td>(N/A)</td>
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</tr>
<tr>
<td>Tetra butyl ammonium chloride</td>
<td>0.1</td>
<td>Average Complex Organic</td>
<td>(N/A)</td>
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<tr>
<td>Toluene</td>
<td>11.7</td>
<td>Solvent</td>
<td>59.7</td>
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<tr>
<td>Triethylamine</td>
<td>2.0</td>
<td>Solvent</td>
<td>13.2</td>
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<tr>
<td>Tropine</td>
<td>1.5</td>
<td>Average Complex Organic</td>
<td>(N/A)</td>
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<tr>
<td>n-Hexane</td>
<td>27.5</td>
<td>Solvent</td>
<td>140.0</td>
<td></td>
</tr>
</tbody>
</table>

### Metrics

- **Mass Intensity**: 184.7 (Sum of the mass of all input materials.)
- **Mass Productivity**: 0.5%  
  (100 / Mass Intensity)
- **Solvent Score**: 1.7  
  (Solvent Score may be less than 1.)
- **RME**: 14%  
  (Reactant Mass Equivalence is calculated by 100 / (mass of reactants);)

---

Measure of chemistry efficiency

Measure of resource efficiency
### Material Impact Assessment Report

#### Detailed Report

<table>
<thead>
<tr>
<th>Material</th>
<th>Weight/kg</th>
<th>Classification</th>
<th>Mass Net</th>
<th>Gross Energy</th>
<th>POCP</th>
<th>GHG</th>
<th>ACIDN</th>
<th>EUTROPN</th>
<th>TOC</th>
<th>OIL</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-methyl-2-amino-1-propanol</td>
<td>1.2</td>
<td>Average Complex Organic</td>
<td>6.95</td>
<td>139</td>
<td>0.0</td>
<td>10</td>
<td>0.31</td>
<td>0.09</td>
<td>0.1</td>
<td>5</td>
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<tr>
<td>3'-chloropropiophenone</td>
<td>0.9</td>
<td>Average Complex Organic</td>
<td>5.19</td>
<td>104</td>
<td>0.0</td>
<td>7</td>
<td>0.23</td>
<td>0.07</td>
<td>0.1</td>
<td>4</td>
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<tr>
<td>Bromine</td>
<td>0.9</td>
<td>General Inorganic</td>
<td>1.06</td>
<td>44</td>
<td>0.0</td>
<td>4</td>
<td>0.04</td>
<td>0.00</td>
<td>0.0</td>
<td>2</td>
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<tr>
<td>DTTA</td>
<td>3.2</td>
<td>Complex Organic</td>
<td>0.50</td>
<td>172</td>
<td>0.0</td>
<td>10</td>
<td>0.68</td>
<td>0.02</td>
<td>0.3</td>
<td>7</td>
</tr>
<tr>
<td>Ethyl acetate</td>
<td>48.2</td>
<td>Solvent</td>
<td>34.79</td>
<td>2,000</td>
<td>0.7</td>
<td>201</td>
<td>1.45</td>
<td>0.55</td>
<td>5.2</td>
<td>52</td>
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<tr>
<td>Hydrochloric acid</td>
<td>0.1</td>
<td>General Inorganic</td>
<td>0.08</td>
<td>1</td>
<td>0.0</td>
<td>0</td>
<td>0.00</td>
<td>0.00</td>
<td>0.0</td>
<td>0</td>
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<tr>
<td>IMS</td>
<td>1.5</td>
<td>Solvent</td>
<td>0.00</td>
<td>40</td>
<td>0.0</td>
<td>4</td>
<td>0.02</td>
<td>0.00</td>
<td>0.0</td>
<td>1</td>
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<tr>
<td>IPA</td>
<td>0.2</td>
<td>Solvent</td>
<td>0.30</td>
<td>11</td>
<td>0.0</td>
<td>1</td>
<td>0.01</td>
<td>0.00</td>
<td>0.0</td>
<td>1</td>
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<tr>
<td>Methanol</td>
<td>0.2</td>
<td>Solvent</td>
<td>0.15</td>
<td>4</td>
<td>0.0</td>
<td>0</td>
<td>0.00</td>
<td>0.00</td>
<td>0.0</td>
<td>0</td>
</tr>
<tr>
<td>Potassium carbonate</td>
<td>1.0</td>
<td>Average Metal Cation Inorganic</td>
<td>1.46</td>
<td>15</td>
<td>0.0</td>
<td>1</td>
<td>0.01</td>
<td>0.00</td>
<td>0.0</td>
<td>1</td>
</tr>
<tr>
<td><strong>Sum</strong></td>
<td><strong>55.3</strong></td>
<td></td>
<td><strong>58.49</strong></td>
<td><strong>2,528</strong></td>
<td><strong>0.7</strong></td>
<td><strong>247</strong></td>
<td><strong>2.76</strong></td>
<td><strong>0.74</strong></td>
<td><strong>5.8</strong></td>
<td><strong>71</strong></td>
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<tr>
<td><strong>Score</strong></td>
<td><strong>3.4</strong></td>
<td></td>
<td><strong>2.9</strong></td>
<td><strong>2.8</strong></td>
<td><strong>3.4</strong></td>
<td><strong>3.0</strong></td>
<td><strong>2.6</strong></td>
<td><strong>1.8</strong></td>
<td><strong>3.4</strong></td>
<td></td>
</tr>
<tr>
<td><strong>STAR</strong></td>
<td><strong>2.9</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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What if Analysis

Fast Lifecycle Assessment for Synthetic Chemistry (FLASC)

What If Analysis Report

What If Analysis

Listed below is the selected WRAP assessment with the What If Analysis details. A maximum of 4 What If Entries can be entered.

Summary Details

Create New What If  Clear What If Entries

Scoring Breakdown

<table>
<thead>
<tr>
<th>Route</th>
<th>Score</th>
<th>MI</th>
<th>MP%</th>
<th>SScore</th>
<th>RME%</th>
</tr>
</thead>
<tbody>
<tr>
<td>62b3</td>
<td>2.9</td>
<td>55.3</td>
<td>1.8%</td>
<td>9.5</td>
<td>N/A</td>
</tr>
<tr>
<td>Scenario 2</td>
<td>3.5</td>
<td>32.1</td>
<td>3.1%</td>
<td>9.0</td>
<td>N/A</td>
</tr>
</tbody>
</table>

* denotes original Route.
FLASC™ by the Numbers

- More than 500 FLASC assessments completed to date
- 229 materials currently in FLASC db.
  - ~70 additional LCIs completed, to be added during 2008
  - For materials not in the database, average data is inserted based on classification of the raw materials into 14 groups of chemicals having related LCI impact profiles
- 22 GSK benchmark processes used to developed FLASC methodology and score
- 10 screening questions to identify opportunities for process improvement are included
- 5-to-1 Score (low is bad, high is good)
- 2 sets of data required as input: route’s BOM (materials and masses) & API’s MW
### Case Study: Comparison of Multi-Column Chromatography (MCC) vs. Dynamic Kinetic Resolution (DKR) for the GW353162A Process

The use of Multi-Column Chromatography (MCC) for physically resolving the racemate in the synthesis of GW353162A is compared with the chemical route B3 using Dynamic Kinetic Resolution.

<table>
<thead>
<tr>
<th></th>
<th>Environment</th>
<th>Safety</th>
<th>Efficiency</th>
<th>Energy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dynamic Kinetic</td>
<td>Yellow</td>
<td>Yellow</td>
<td>Yellow</td>
<td>Red</td>
</tr>
<tr>
<td>Resolution</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multi-Column</td>
<td>Green</td>
<td>Green</td>
<td>Green</td>
<td>Yellow</td>
</tr>
<tr>
<td>Chromatography</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Color Key:**
- Green: alternatives with significant advantages
- Yellow: alternatives with significant disadvantages
- Red: alternatives that do not exhibit significant advantages or disadvantages

*For the Environment category, mass indicators and life cycle indicators were considered. For the Energy category, energy requirements and life cycle energy were considered.*

---

**Source:** Eco-Design Toolkit

**Methodology:**
For instance…

**LCI/A comparison for:**
- recovery of THF
- Dehydration of alcohols
- Resolution of enantiomers
- Concentration of mother liquors
- And more…
How green is your pack?

The Green Packaging Guides and WRAP - (Wizard for the Rapid Assessment of Packaging) can help you find out.

The GSK Green Packaging Guides consist of GSK pack benchmarks for different product types and Best Example for each category. The guides not only take into account the packaging but also the product it contains.

- Nutritional Healthcare Green Packaging Guide.
- Consumer Healthcare Green Packaging Guide.

You cannot make direct comparisons across Guides since the nature of the product often restricts packaging options and consequently makes inter-guide comparisons invalid.

WRAP will evaluate your pack using the same criteria as the benchmarks. This means you can tell if your pack is better or worse than our current packs and compare this with the Best Example.

Your assessments will be tracked using your LAN ID: cjj10486

Enter WRAP  Administration Module
Other LCI/A Applications in GSK
End-of-Life: Waste Treatment Modules

Example – THF Solvent Recovery vs Energy Recovery

Manufacturing Plant Case 1

1,000 kg THF

Incinerator with 50% Energy Recovery

~ 3,570 kg CO₂-eq

Manufacturing Plant Case 2

800 kg THF

Solvent Recovery

1,000 kg THF

Incinerator w/Energy Recovery

~ 1,060 kg CO₂-eq

200 kg

~ 10,000 kg CO₂-eq SAVINGS from manufacturing

Approx Estimated Savings ~12,000 kg CO₂-eq
Bio-processes, closing the cycle – A sustainable vision?
Bio-Processes GSK Case Study – LCA of 7ACA

Materials (FLASC) → Chemical Process → 7-ACA
- Waste treatment
- Energy production

Materials (FLASC) → Enzymatic Process → 7-ACA
- Waste treatment
- Energy production

API production, formulation, distribution and consumption
Comparing Chemical (C) and Enzymatic (E) Routes

Source:
Assessing the environmental life cycle impacts of products.

Evaluate Devices for opportunities to reduce their environmental footprint.

GSK Pilot Program for Delivery Device Recycling.

- **Materials**
  - It includes raw material extraction and transformation.

- **Production**
  - It comprises the production and assembly process.

- **Transport**
  - It accounts for transport from suppliers and to markets.

- **Use**
  - It includes Device use.

- **End of Life**
  - It accounts for treatment, Disposal and recycling.
LCA impacts applied to in GSK-CH’s Mission and Targets

Our Environmental Sustainability Mission:
Grow our business whilst continuously improving our environmental impact

- Packaging
  -25% packaging weight
  100% recyclable packs
  50% recycled content

- Sustainable Ingredients
  Sustainable sourcing strategy for major ingredients

- Energy & Emissions
  -20% Energy usage & Global Warming Potential

- Water
  -20% Water Usage Ratio

- Waste
  -1% / year non-hazardous solid waste
The Road Ahead

Continue embedding LCI/A in evaluations and tools:
- NCEs and Key products,
- processes with fermentation and enzymation
- End of life considerations

Enhance and Update our tools
- Solvent Selection Guide
- FLASC
- Green Packaging Guide

Benchmark
- With other Pharma (e.g. AZ)
- Other industries Analysis

In the longer term need to incorporate
- human health,
- ecotoxicity,
- principles of inherent safety,
- and economics.
Acknowledgements

- Alan Curzons, GSK CEHSS, ret.
- Rebecca DeLeeuwe, GSK CEHSS
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- Jim McCann, GSK Corporate IT
- Teresa Oliveira, GSK R&D
- Mark Rhodes, GSK CEHSS
- Brian Rohrback, Infometrix
- Tom Roper, GSK R&D
- Clare Ruddick, GSK R&D
- GSK’s Sustainable Processing Team
- GSK’s staff in Corporate EHSS and Chemical Development
Any Questions?

...Others make it happen!
Back up slides
If we want to make the **biggest impacts to products, services and costs**, we have to start from the ground up.

If we want to **build sustainability into the design of products and services** we have to think differently about the what and how of R&D.

Increasing demands and decreasing budgets are likely to mean greater reliance on easily accessible company-wide tools that provide **early** assessments and highlight **sustainability issues**.
Key Deliverables of LCI/A of API

- A generic ‘life cycle approach’ applicable to:
  - strategic decision making,
  - business processes and
  - other processes and tools

- Generic learnings on life cycle and Pharmaceuticals

- A documented *Simplified methodology*

- A LCI/A component for the *Solvent Selection Guide*

- **FLASC** - Fast Life cycle Assessment of Synthetic Chemistry
LCA of API pre-treatment results

- Eutrophication (2.75 PO4-3-eq.)
- Acidification (8.36 SO2-eq)
- GHG (979 CO2-eq)
- POCP (3.96 kg-et)
- TOC (14.8 kg)
- Energy (8,359.5 MJ)
- Total cradle materials (678.11 kg)

0% 20% 40% 60% 80% 100%

Process
Energy
Transport
LCA of API post-treatment results

- Total cradle materials: 799.46 kg
- Energy: 13,084 MJ
- TOC: 2.1 kg
- POCP: 2.18 kg-et
- GHG: 1,836 CO2-eq
- Acidification: 9.08 SO2-eq
- Eutrophication: 1.32 PO4-3-eq
- Spent solvent: 154 kg

The diagram shows the contribution of each category to the overall LCA results, with the process, energy, transport, and treatment categories represented.
How FLASC™ was developed

Eight core impact categories established

Life Cycle based environmental data were first developed for materials (NCSU’s Modular Approach), then for processes to a large number of GSK’s APIs

This data set is used as a benchmark for assessing new processes using a comparative scoring process

Combined single ‘FLASC™’ score is generated, corrected for COMPLEXITY of drug substance molecule

<table>
<thead>
<tr>
<th>Process</th>
<th>Mass</th>
<th>Energy</th>
<th>POCP</th>
<th>Acid</th>
<th>Eutr</th>
<th>Oil</th>
<th>GHG</th>
<th>TOC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>100</td>
<td>855</td>
<td>5</td>
<td>1</td>
<td>2</td>
<td>80</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>2</td>
<td>150</td>
<td>800</td>
<td>4</td>
<td>15</td>
<td>3</td>
<td>50</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>3</td>
<td>200</td>
<td>1500</td>
<td>9</td>
<td>11</td>
<td>1</td>
<td>125</td>
<td>12</td>
<td>12</td>
</tr>
</tbody>
</table>

Process Score 1 Score 2 Score 3 Score 4 Score 5 Score 6 Score 7
NEW 4 4.1 1.9 4.5 3.9 4.1 3.8

4.1
Detailed Report (biggest contributors)

Fast Lifecycle Assessment for Synthetic Chemistry (FLASC)

The Biggest Contributors

Listed below are the materials that influence the STAR rating the most compared with all the materials in your route in terms of mass and energy. In order to improve the environmental profile of your route you should concentrate on these materials by either replacing them or reducing the mass required.

Largest Mass Contributors

<table>
<thead>
<tr>
<th>Material</th>
<th>Class</th>
<th>% Contribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethyl acetate</td>
<td>Solvent</td>
<td>59</td>
</tr>
<tr>
<td>DTTA</td>
<td>Complex Organic</td>
<td>15</td>
</tr>
<tr>
<td>2-methyl-2-amino-1-propanol</td>
<td>Average Complex Organic</td>
<td>12</td>
</tr>
</tbody>
</table>

Largest Energy Contributors

<table>
<thead>
<tr>
<th>Material</th>
<th>Class</th>
<th>% Contribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethyl acetate</td>
<td>Solvent</td>
<td>79</td>
</tr>
<tr>
<td>DTTA</td>
<td>Complex Organic</td>
<td>7</td>
</tr>
<tr>
<td>2-methyl-2-amino-1-propanol</td>
<td>Average Complex Organic</td>
<td>5</td>
</tr>
</tbody>
</table>
Developing the LCA Dataset

- **Cradle-to-gate LCI** in GSK’s guide
- **LCA using GSK’s metrics**
  - *Net mass of materials used* (kg)
  - *Energy required* (MJ)
  - *Greenhouse gas equivalents* (kg of CO₂-equivalents)
  - *Oil and natural gas depletion for materials manufacture* (kg)
  - *Acidification potential* (AP, kg of SO₂ equivalents)
  - *Eutrophication potential* (EP, kg of (PO₄)-3 equivalents)
  - *Photochemical ozone creation potential* (POCP, kg of ethylene-equivalents)
  - *Total organic carbon (TOC) load before waste treatment*
• FLASC tracks MP very well for most processes (real value of measuring MP)

• Two key advantages of FLASC – it takes into account starting material and product complexity.

• Where SMs are complex FLASC takes this into account - this is why there are outliers.
PCA for selected inorganic materials

- Sodium methoxide
- Aluminium chloride
- Magnesium sulphate
- Sodium nitrite
- Ammonium fluoride
- Sodium hydroxide
- Calcium carbonate
- Potassium hydroxide
- Lithal
- Lithium carbonate
- Lithium chloride
- Lithium
<table>
<thead>
<tr>
<th>FLASC rating</th>
<th>% Relative to the average</th>
<th>Comments.</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.0</td>
<td>12%</td>
<td></td>
</tr>
<tr>
<td>4.3</td>
<td>20%</td>
<td></td>
</tr>
<tr>
<td>4.0</td>
<td>25%</td>
<td>For a FLASC™ score = 4, the total Life Cycle mass and energy associated with the materials used is 25% of that associated with an average route.</td>
</tr>
<tr>
<td>3.8</td>
<td>30%</td>
<td></td>
</tr>
<tr>
<td>3.4</td>
<td>40%</td>
<td></td>
</tr>
<tr>
<td>3.1</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td>2.9</td>
<td>60%</td>
<td></td>
</tr>
<tr>
<td>2.7</td>
<td>70%</td>
<td></td>
</tr>
<tr>
<td>2.5</td>
<td>80%</td>
<td></td>
</tr>
<tr>
<td>2.4</td>
<td>90%</td>
<td></td>
</tr>
<tr>
<td>2.3</td>
<td>100%</td>
<td>25 GSK routes developed during 1990 to 2000 were assessed. The average Life Cycle environmental impact was assigned a rating of 2.3.</td>
</tr>
<tr>
<td>2.1</td>
<td>110%</td>
<td></td>
</tr>
<tr>
<td>2.0</td>
<td>120%</td>
<td>For a FLASC™ score = 2 the total Life Cycle mass and energy use associated with the materials is 120% relative to the average route</td>
</tr>
<tr>
<td>1.9</td>
<td>130%</td>
<td></td>
</tr>
<tr>
<td>1.7</td>
<td>150%</td>
<td></td>
</tr>
<tr>
<td>1.4</td>
<td>200%</td>
<td></td>
</tr>
<tr>
<td>1.0</td>
<td>300%</td>
<td>For a score = 1 the life cycle mass and energy associated with the materials is 300% relative to the average route</td>
</tr>
</tbody>
</table>
Example 2 – Recovery, Segregation and Treatment

Manufacturing Plant Case 1

500 kg DCM
500 kg MeOH/Water (50:50)

Manufacturing Plant Case 2

500 kg DCM
500 kg MeOH/Water (50:50)

~ 1,380 kg CO₂-eq

~ 370 kg CO₂-eq

Solvent Recovery

Incinerator without Energy Recovery

Solvent Recovery

WWTP

Incinerator w/o ER

~ 375 kg DCM

56 kg MeOH

25 kg MeOH

Approx Estimated Savings ~1,000 kg CO₂-eq
GSK’s R&D Green Metrics

- Set of agreed green metrics for synthetic route development:
  - FLASC Score
  - Solvent Score
  - Mass Productivity
  - Reaction Mass Efficiency
  - Mass Intensity
  - Number and mass of solvents
  - Materials of Concern
  - Mass of water
  - Major contributors to total mass

- Calculated and communicated at every Pilot Plant Campaign
- Provides Benchmark of routes in same stage of development
- Includes guidance and targets
Process Related Materials Review

- A single file with the EHS information for a whole process
- Provides EHS information and key issues for synthetic routes
  - Captures an agreed set of green metrics, including FLASC & Solvent Score, MP, RME
- Is produced at 3 milestones of product development.

- Preliminary measure of EHS/ green chemistry performance.
- Identifies and communicates issues and opportunities for more sustainable chemistry and technology
GSK CEO’s EHS Excellence Awards

- Promotes improvements in GSK’s use of human, environmental and economic resources
- Recognizes innovation, effective over the long-term, that can be shared within GSK
- Three categories
  - EHS Community Partnership
  - Green Chemistry / Technology
  - EHS Initiative (H&S)

- FLASC & Solvent Scores are common metrics used by the teams submitting Award entries in the Green Chemistry / Green Technology category
Measuring Progress: Development Portfolio

The environmental life cycle impact of all new processes post-PoC is potentially much lower than for current processes in manufacturing.

* The average performance of the benchmark routes (1990-2000) was assigned a FLASC score of 2.3
Results: Materials Impacts

- Using GSK’s FLASC™ tool to compare the two routes

### Route Assessment

<table>
<thead>
<tr>
<th>Scores</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Chem</td>
<td>2.7</td>
<td>3</td>
</tr>
<tr>
<td>bio</td>
<td>23%</td>
<td></td>
</tr>
</tbody>
</table>

### Score Benchmarking

- Best
- Unacceptable

The % value shown is the improvement (reduction in environmental impacts) compared to the worst route selected.

<table>
<thead>
<tr>
<th>Routes Evaluated (Graph Name)</th>
<th>MW</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>7-ACA chem July 07 (Chem)</td>
<td>272.27</td>
<td>chem route - Mass Bal Checked 16-7-07</td>
</tr>
</tbody>
</table>